

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : James A. Laugharn, Jr. et al. Art Unit : 1744  
Serial No. : 10/770,241 Examiner : Elizabeth L. McKane  
Filed : February 2, 2004 Conf. No. : 9463  
Title : RAPID CRYOBARIC STERILIZATION AND VACCINE PREPARATION

**Mail Stop Appeal Brief - Patents**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**BRIEF ON APPEAL**

**(1) Real Party in Interest**

Pressure Biosciences, Inc. is the Real Party in Interest and was formerly known as Boston Biomedica, Inc. including its wholly owned subsidiary BBI Bioseq, Inc.

**(2) Related Appeals and Interferences**

There are no prior or pending appeals, interferences, or judicial proceedings related to the present application.

**(3) Status of Claims**

Claims 3-5, 8, and 15-31 are cancelled.

Claims 1, 2, 6, 7, 9-14, and 32-37 are pending.

Claims 1, 2, 6, 7, 9-14, and 32-37 are pending. Claim 1 is the only pending independent claim. All of the claims stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Hashizume et al. "Kinetic Analysis of Yeast Inactivation by High Pressure Treatment at Low Temperatures" ('Hashizume') in view of Hayakawa et al. "Oscillatory Compared with Continuous High Pressure Sterilization on Bacillus stearothermophilus Spores" ('Hayakawa').

Claims 7 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants have submitted claim amendments, which have not yet been entered, addressing these rejections.

Claims 32 and 33 are objected to due to a misspelling of the word "macromolecule." Applicants have corrected this typographical error in the amendment filed but not yet entered.

**(4) Status of Amendments**

Editorial amendments to claims 7, 32, 33, and 36 were submitted on October 23, 2006, but were not entered by the Examiner because Applicants made errors in that amendment. The appendix of claims attached hereto contains the correct listing of the claims as they existed before the amendment of October 23, 2006. On January 10, 2008, Applicants submitted an amendment correctly showing changes to the pre-October 23, 2006 claims and making the editorial amendments sought to be made on that date.

**(5) Summary of Claimed Subject Matter**

The claims recite methods of sterilizing a material. (See e.g., page 3, lines 23-26.) The methods include providing the material at an initial pressure, and while maintaining the material in a temperature range below 45 °C, (See e.g., page 3, line 23 to page 4, line 1.) increasing the pressure to an elevated pressure, and then decreasing the pressure below the elevated pressure and cycling the pressure between a decreased pressure and the elevated pressure at least two times to provide a sterilized material. (See e.g., page 5, lines 1-5.)

**(6) Grounds of Rejection**

Claims 1, 2, 6, 7, 9-14, and 32-37 stand rejected under 35 U.S.C. § 103(a) as being obvious and therefore unpatentable over the combination of Hashizume in view of Hayakawa.

Claims 7 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 32 and 33 are objected to due to a misspelling of the word "macromolecule."

**(7) Argument**

Claims 1, 2, 6, 7, 9-14, and 32-37 are not obvious and therefore unpatentable over the combination of Hashizume and Hayakawa.

The pending claims recite methods of sterilizing a material by subjecting the material to cycled pressure (i.e., cycling between elevated pressure and decreased pressure) and maintaining the temperature of the material below 45 °C.

Hashizume discloses methods of inactivating *Saccharomyces cerevisiae* (a strain of yeast), using high pressure treatment. Hashizume says that “rapid inactivation took place when the temperature was above 45 °C or below -10 °C.” (See Hashizume page 1456, lines 17-19, left column.) Hashizume does not teach or suggest cycling pressure between an increased and decreased pressure, nor is Hashizume relied upon for such a teaching.

Hayakawa discloses examples of the use of oscillatory pressurization (i.e., pressure cycling) to reduce the count of thermoduric spores of *Bacillus stearothermophilus*. Hayakawa tested the effects of oscillatory pressurization on spores, demonstrating that “(o)scillatory pressurization at 70 °C completely burst each spore along the length of the spore shape.” (See Hayakawa, p. 165 and 166, RESULTS, Oscillatory pressurization, and Figure 5.)

When applying 35 U.S.C. 103, the following tenets of patent law must be adhered to: (A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) Reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

Applicants have limited the claimed invention to methods of sterilizing material at temperatures below 45 °C using cycled pressure. The references, when considered as a whole, do not fairly teach Applicants' claimed methods. The Examiner cites Hayakawa as the only example of using cycled pressure, and yet the temperatures used in Hayakawa fall outside Applicant's claimed ranges. Moreover, as demonstrated in Figure 3 of Hayakawa, increasing the temperature from 60 °C to 70 °C with oscillatory pressure led to a greater reduction in survivors at two different pressures (i.e., 400 MPa and 600 MPa).

Without the benefit of impermissible hindsight afforded by Applicants' claimed invention, one would not arrive at methods for sterilizing material at temperatures below 45 °C using cycled pressure. Instead, one would be motivated to use the methods clearly taught by

Hayakawa. While the Examiner asserts that one would be motivated to modify the teachings of Hashizume with Hayakawa to arrive at the claimed invention, the references, when taken as a whole, more fairly suggest methods of oscillatory pressure at elevated temperatures, i.e., temperatures greater than 45 °C, such as 60 °C or 70 °C. Moreover, nothing in the combined references would provide an expectation of success when practicing the claimed invention. Rather, Hashizume notes that "No or little inactivation was observed for the pressureization below 180 MPa at temperatures between 0 °C and 40 °C." (See Hashizume page 1456, lines 17-19, left column.)

Claims 7 and 36 are rejected under 35 U.S.C. 112, second paragraph.

Applicants have submitted claim amendments, which have not yet been entered, addressing these rejections. These rejections will be moot upon entry of these amendments.

Claims 32 and 33 are objected to due to a misspelling of the word "macromolecule."

Applicants have submitted claim amendments, which have not yet been entered, addressing these objections. These objections will be moot upon entry of these amendments.

Conclusion

Applicants submit that the cited references, when taken as a whole, fail to suggest the claimed methods and therefore the claimed methods are patentable over the cited references. Applicants therefore request that the rejection be withdrawn and the application be placed in condition for allowance.

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The brief fee was submitted with the earlier filed Appeal Brief. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket no 07985-031002.

Respectfully submitted,

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Date: September 12, 2008

### Appendix of Claims

1. A method for sterilizing a material, the method comprising:
  - providing said material at an initial pressure; and
  - while maintaining said material in a temperature range that is below 45°C, increasing the pressure to an elevated pressure, then decreasing the pressure below the elevated pressure, and cycling the pressure between a decreased pressure and the elevated pressure at least two times, thereby providing a sterilized material.
2. The method of claim 1, wherein the material is provided at an initial pressure of about 1 atm.
6. The method of claim 1, wherein the elevated pressure is in the range of about 5,000 psi to about 120,000 psi.
7. The method of claim 1, wherein the desired biomolecule is selected from the group consisting of nucleic acids, proteins, lipids, carbohydrates, drugs, steroids, and nutrients.
9. The method of claim 1, wherein the pressure is cycled at least ten times.
10. The method of claim 1, wherein the decreased pressure is half of the elevated pressure or less.

11. The method of claim 1, further comprising warming or cooling the material prior to the pressure-increasing step.

12. The method of claim 1, further comprising warming or cooling the material after the pressure-increasing step.

13. The method of claim 1, wherein the material being sterilized is selected from the group consisting of a biological sample; blood plasma, serum, or other plant, animal, or human tissue; feces; urine; sputum; medical or military equipment; a foodstuff; a pharmaceutical preparation; ascites; and a vaccine.

14. The method of claim 1, wherein the material being sterilized is initially contaminated with at least one of a prion, a virus, a fungus, a protist, a nucleic acid, and a protein.

32. The method of claim 1 in which the sterilized material comprises a desired marcmolecule.

33. The method of claim 14 in which the sterilized material comprises a desired marcmolecule.

34. The method of claim 32 in which the desired macromolecule has a biological activity that is maintained in the sterilized material produced by the method.

35. The method of claim 32 in which the macromolecule is a protein.

36. The method of claim 32 in which the infectious agent is a virus.

37. The method of claim 1, wherein the elevated pressure is in the a range of about 2,000 psi to about 120,000 psi.

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### **Evidence Appendix**

None.

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**Related Proceedings Appendix**

None.